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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/087,633	03/01/2002	Tatsuya Yano	02012CIP/HG	3745

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EXAMINER
HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 02/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/087,633	YANO ET AL.	
	Examiner	Art Unit	
	Susan Hanley	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) *13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 14-32* is/are rejected.

7)☒ Claim(s) *1-4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/1/02 and 1/6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Election/Restrictions

Applicant's election with traverse of claims 1-4, 14-17 and 30 in the response received on January 6, 2004 is acknowledged. The traversal is on the ground(s) that groups II and III were classified in the same class, 435. Groups I and IV should be examined together since the product of group I can not be used as an insecticide. Regarding groups I and II, applicant alleges that the product of Group I can not be made by traditional organic synthetic methods.

Claims 1-4, 14-17 and 30 are directed to an allowable product. Pursuant to the procedures set forth in the Official Gazette notice dated March 26, 1996 (1184 O.G. 86), claims 5-12, 18-29 and 31-32, directed to the processes of making and using the patentable product will be rejoined and examined together. However, product claim 13, drawn to a strain of *Phoma*, is not rejoined. Regarding Applicant's argument that Groups I and II are in the same class and should be examined together is not deemed persuasive. It is noted that proper restriction practice requires that the groups have different *classification*. Group III, drawn to a Phoma strain is classified in the 254.1 subclass, while Group III is drawn to a method of making a cyclic antibiotic with the Phoma species, subclass 71.3. The two groups have different classification as well as differing scope. Hence, the search between the two groups is not co-extensive.

In conclusion, Groups I, II and IV, claims 1-12 and 14-32, are rejoined and will be examined together. Group III, claim 13, has NOT been rejoined. Claim 13 is withdrawn from consideration. The requirement for restriction of Group III is still deemed proper and is therefore made FINAL.

Specification

The use of the trademark Shodex Asahipak has been noted in this application. It should be capitalized wherever it appears, noted as a trademark and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

Claims 1-4 are objected to because of the following informalities: There should be a period after each claim number. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-12 and 14-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are drawn to two cyclic peptidyl lactones, compositions thereof, methods of making and methods of using. The cyclic peptidyl lactones can only be made by culturing microorganisms of the strain *Phoma* sp. SANK (FERM BP-6851).

Since said microorganisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganisms of the said strain are not so obtainable or available, the requirements of *35 USC 112*, first paragraph may be satisfied by a deposit of the microorganisms. It is not apparent if the microorganisms are readily available to the public. The specification must contain the date that the microorganism was deposited, the accession number for the microorganism, the name of the microorganism and the address of where the microorganism was deposited. It is noted in the specification (p. 11) that the applicants have deposited the organism but there is no indication if the deposit was made under the terms of the Budapest Treaty or to the conditions of availability of the deposited strains to the public upon issuance of a patent for said strains.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or hers signature and registration number, **stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of a patent**, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in CFR 1.801-809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or hers signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) a restriction upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and,

(d) the deposit will be replaced if it should ever become inviable.

Claims 5-8 and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method of preparation of cyclic peptidyl lactones by the methods of claims by microorganism, *Phoma* sp. SANK (FERM BP-6851), does not reasonably provide enablement for said preparation of said compounds by microorganisms belonging to any possible species or strain of the genus *Phoma.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

Claims 5-8 and 31 are drawn to preparation of the cyclic peptidyl lactones of claims 1-4 by cultivating microorganisms belonging to any possible species or strain of the genus *Phoma.* The specification shows that microorganisms belonging to the strain *Phoma* sp. SANK (FERM BP-6851), are capable of performing the desired biosynthesis. The limited showing of one bacterial strains with a particular activity is not sufficient to enable a claim drawn to all species or stains of the genus to which said bacterium belong.

The specification does not disclose if one skilled in the art can utilize any species or strain of microorganism from the genus *Phoma* to make the claimed compounds with a reasonable expectation of results. A search by the Examiner showed that the ring structure of the claimed compounds is found in four compounds in the Registry file of CAS. There is no reported conventional organic synthetic method for such a ring structure. Hence, it is highly desirable obtain the desired products by a bio-preparative method. However, the formation of cyclic peptidyl lactones by biological means is difficult because said structure does not exist in a main metabolic pathway of living organisms. It appears that the synthetic activity of the

disclosed strains is rare and an individual characteristic of said strain. Hence, one skilled in the art would be unable to pick a species or strain from said genera and expect it to possess the same set of properties. If the method of claims 5-8 and 31 is not generally applicable to any species or strain of the disclosed genera, then the desired biosynthetic activity all possible species of strains of the genus Phoma would be considered individually. This would be considered undue experimentation.

There is no reliable method that predicts which species or strains from the genus *Phoma* have the desired activity to synthesize the claimed compounds described in the specification. A search of the prior art shows that the ring structure of the claimed compounds is unique to four compounds in the Registry file. The specification does not teach how one of ordinary skill in the art could decide *a priori* which sources will provide a microorganism with the desired characteristics. The limited disclosure cannot be extrapolated by the skilled artisan to predict which strains from said genera are capable of biosynthesizing the claimed cyclic compounds. It would require one of ordinary skill in the art undue experimentation to determine what species or strains of the genus Phoma can perform the desired biosynthesis according to the directions of the instant disclosure. Thus, claims 5-8 and 31 are not commensurate in scope with the enabling disclosure.

Claims 18-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating fungal infections caused by:

a. *Cryptococcus neoformans* with the compound of claims 1-2, also referred to in the specification as F-15078A, and the compound of claims 3-4, also referred to as F-15078B; and

b. *Candida albicans and Aspergillus fumigatus* with the compound of claims 1-2, also referred to in the specification as F-15078A,

does not reasonably provide enablement for treatment and/or prevention of fungal diseases caused by any possible fungus by either F-15078A or F-15078B. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The claims are drawn to a method of treating and/or preventing fungal infections with the compounds of claims 1-4, also referred to as F-15078A and F-15078B. The specification discloses that F-15078A inhibits *Candida albicans, Aspergillus fumigatus* and *Cryptococcus neoformans*, while F-15078B appears to inhibit the growth of only *C. neoformans.* It is unclear if F-15078B inhibits *Candida albicans* or *Aspergillus fumigatus.* The specification discloses that the minimum inhibitory concentration (MIC) of F15078B required to inhibit *Candida albicans and Aspergillus fumigatus* is greater than 50 ug/mL. There is no upper limit to this concentration. Since the MIC for F15078B for these two microorganisms is not established, it is unclear is F15078B would be effective in treating or preventing infections caused by said microorganisms. However, there is no disclosure related the treatment and/or prevention of any possible fungal infection with any of the compounds of claims 1-4. The limited showing of the inhibition of fungal activity of *Candida albicans, Aspergillus fumigatus* by F15078A, and *Cryptococcus neoformans* by F15078A or F15078B is not sufficient to enable a claim drawn to the treatment and/or prevention of any possible fungal infections, with F15078A and F15078B because the arts of biochemistry and medicine are too unpredictable.

The specification does not disclose if one skilled in the art can utilize the claimed composition to prevent and/or treat any possible disease of fungal origin with a reasonable expectation of results. There are a number of diseases caused by various fungi with distinct

causes and etiologies. The prior art, The Merck Manual, shows that there is no single antifungal agent that can treat every possible fungal infection. For example, ketoconazole or amphotericin B is effective in for treating systemic candidiasis (p. 108-109). However, The Merck Manual recommends potassium iodide for the treatment of *Sporothrix* infections (p. 110). Hence, the prior art does not support the idea that any one antifungal agent can prevent and/or treat any possible fungal disease.

It is not clear that the results disclosed for F15078A and F15078B in the instant application can be extrapolated to the prevention and/or treatment of different fungal infections that are not described in the specification. The specification shows that only F15078A inhibits the fungal activity of *Candida albicans* and *Aspergillus fumigatus*, and that *Cryptococcus neoformans* is inhibited by either F15078A or F1507BA. The specification does not show that the claimed composition provides blanket treatment for any type of fungal infection. Nor does the prior art support the notion that a single antifungal can successfully treat any possible fungal infection. Hence, the treatment of fungal infections is reduced to trial and error with potential medications because the prior art discloses that the ordinary artisan cannot easily predict which fungal infections can be successfully by a new antifungal agent and the instant specification does not fill this gap of knowledge.

Further, it is asserted that F15078A or F15078B can *prevent* any fungal disease. The assertion is not backed up by data. Indeed, it would be difficult to obtain data to show that a medicament is keeping a person from contracting a disease. Prevention is the reduction of the predisposition of an individual to a disease. "Predisposition" means to make someone inclined to favor something in advance. The specification is enabled for treating infections caused a) *Cryptococcus neoformans* with F15078A or F15078B, and b) *Candida albicans* and *Aspergillus fumigatus* with F15078A. The specification does not teach how the ordinary artisan would know

in advance if one were predisposed to a condition. Even if the ordinary did know if an individual were predisposed to contract a disease, it is unclear how the artisan would determine a reduction in the likelihood of a disease that an individual may contract or exhibit at some time in the future.

Claims drawn to pharmaceutically acceptable compositions and to methods of administering said compositions to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments. The specification supports the use of the claimed composition for the treatment infections caused a) *Cryptococcus neoformans* with F15078A and F15078B, and b) *Candida albicans* and *Aspergillus fumigatus* with F15078A. However, neither the prior art nor the instant specification support the notion that any antifungal is efficacious for treating any possible fungal infection such that a person of ordinary skill in the art to obtain similar results with any possible fungal disease. Hence, the ordinary artisan would be unable to predict an effective therapy using the claimed composition in the treatment or prevention of a fungal disease not specifically supported by the specification and expect to obtain similar clinical results. If the use of the claimed compounds is not generally applicable for preventing or treating any possible fungal illness, then the treatment of said illness with said composition would have to be considered individually. This would be considered undue experimentation. Similarly, Applicant has not demonstrated that the claimed composition can prevent any fungal disease for the reasons stated *supra*. Thus, claims 18-29 are not commensurate in scope with the enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 4 and 30 contain the trademark/trade name Shodex Asahipak. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe an HPLC column and, accordingly, the identification/description is indefinite.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. The phone number for Technology Center 1600 is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JEAN C. WITZ
PRIMARY EXAMINER